

# Multi-Omics Uncovers Factors Conferring Resistance to Osimertinib in EGFR Positive Non-Small Cell Lung Cancer

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## Conclusions

- Longitudinal plasma profiling demonstrates a potential usability of plasma-derived exosomal RNAs and circulating proteins to characterize molecular phenotypes of emerging osimertinib resistance.
- Longitudinal plasma transcriptome and proteome profiling highlights the involvement of multiple RNA and protein species in shaping the landscape of osimertinib-refractory NSCLC.

## Introduction

Osimertinib is used in the first-line setting for NSCLC patients with activating mutations in EGFR. Here we aimed to analyze if circulating RNAs and proteins, isolated from longitudinally sampled plasma of osimertinib-treated EGFR+ NSCLC patients (baseline and disease progression), could provide signatures of acquired resistance to osimertinib.

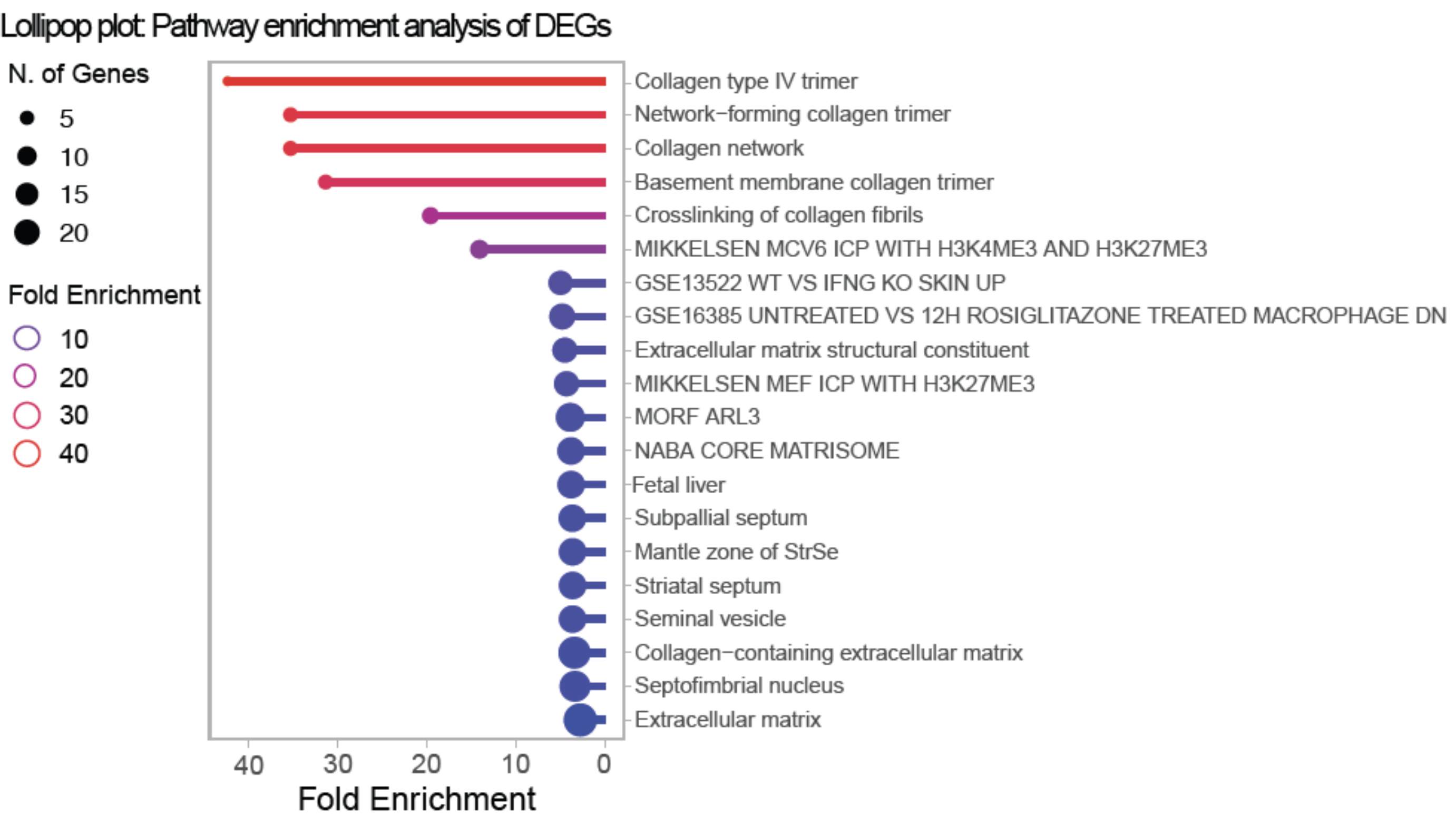


Figure 3. Pathway enrichment analysis of differentially expressed genes of the RNA-landscape in liquid biopsies obtained at treatment baseline or following progression of disease in EGFR-mutant NSCLC patients treated with osimertinib.

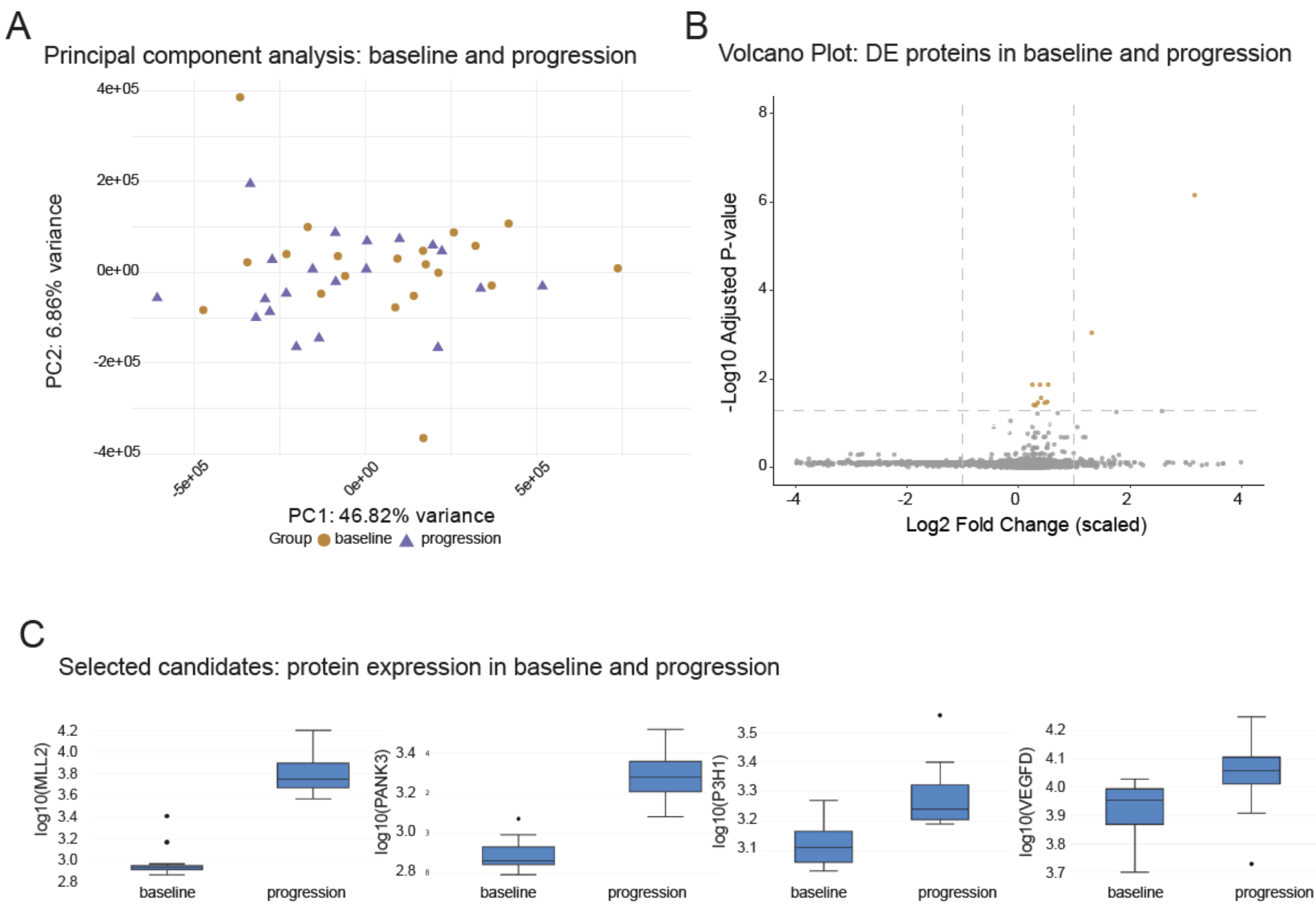


Figure 1. Molecular deciphering of the protein landscape in liquid biopsies obtained at treatment baseline or following progression of disease in EGFR-mutant NSCLC patients treated with Osimertinib. (A) PCA-plot visualizing the overall characteristics of the baseline and progression of disease samples. (B) Volcano-plot displaying the most differentially expressed genes. (C) Selected candidates displaying protein expression in baseline vs progression samples.

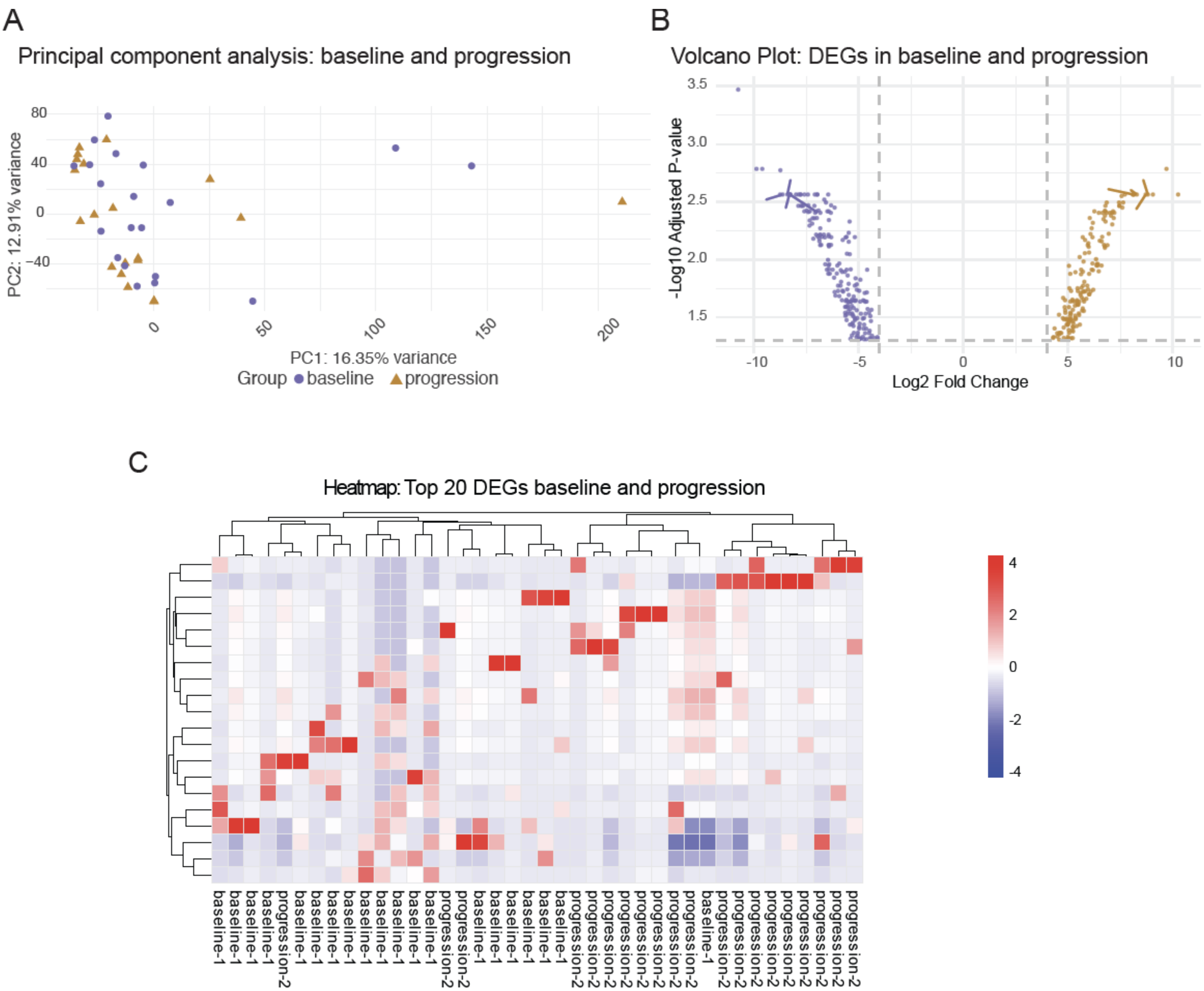


Figure 2. Molecular deciphering of the RNA-landscape in liquid biopsies obtained at treatment baseline or following progression of disease in EGFR-mutant NSCLC patients treated with Osimertinib. (A) PCA-plot visualizing the overall characteristics of the baseline and progression of disease samples. (B) Volcano-plot displaying the most differentially expressed genes. (C) Heatmap displaying the top 20 differentially expressed genes between baseline and progression of disease samples.

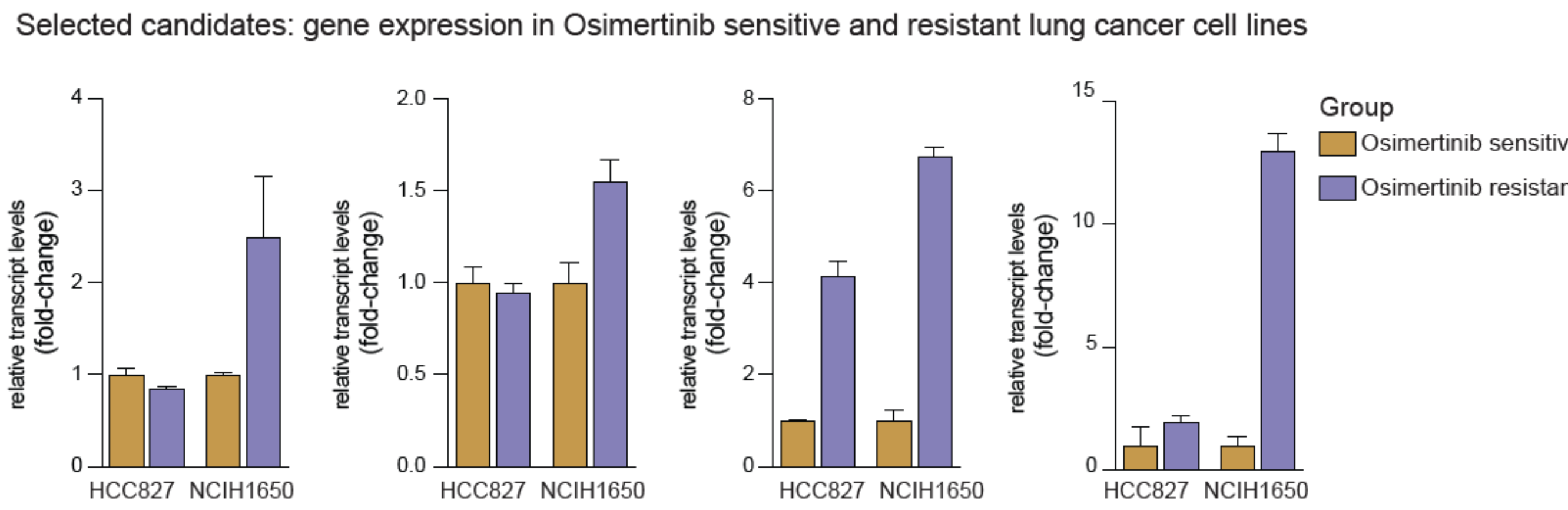


Figure 4. Expression of selected candidates from proteome and transcriptome profiling in Osimertinib sensitive versus Osimertinib resistant NSCLC cell lines. Expression is depicted as relative expression compared to a house-keeping gene. Analysis is conducted through RT-qPCR.